

## **REMARKS**

### **Status of the Claims and Amendment**

Upon entry of the present amendment, which is respectfully requested, claims 1 and 7 will be amended. Claims 5-6 and 19-20 were previously canceled. Claims 1-4 and 7-18 are all the claims pending in this application. Claims 1-4, 8-15, 17 and 18 are withdrawn from consideration as being directed to a non-elected invention. Claims 7 and 16 are rejected.

Claim 1 has been amended to be dependent on claim 7.

Claim 7, has been amended to recite that the N-terminal amino acid is pyroglutamic acid, and part (b) has been amended to recite a protein comprising an amino acid sequence having at least 95% identity to the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40. Support for the amendments to claim 7 may be found throughout the specification, for instance, at page 14, paragraph [0032], Table 4 at page 31, Table 7 at page 37, Examples B3 and B4 from the bottom of page 37-39, and the original claims.

No new matter is added.

### **Request for Rejoinder of Claims 1-4, 8-15, and 17-18**

Applicants respectfully request rejoinder of non-elected claims 1-4, 8-15, and 17-18.

Applicants note that method claims 1-4 and 17-18 include all the limitations of the allowable product claims, and may be rejoined pursuant to M.P.E.P. §821.04(b).

With regard to claims 8-15, which are respectively directed to the polynucleotide, expression vector, host cell, and process of making the claimed protein, Applicants note that rejoinder of the claims is proper pursuant to the PCT International Search and Examination Guidelines (see <http://www.wipo.int/pct/en/texts/gdlines.htm>) on Unity of Invention under PCT



Rule 13. The Examiner is reminded that when protein X and a DNA encoding protein X share a corresponding special technical feature, as in the present case, protein X and the DNA encoding protein X have unity of invention. This is specifically demonstrated in Example 39 of Chapter 10 at 10.59 of the Guidelines, which shows that where a “[p]rotein and its [e]ncoding DNA,” have no prior art against the DNA or protein, “the claims have unity of invention ... protein X and the DNA encoding protein X share a special technical feature.”

Accordingly, rejoinder of claims 1-4, 8-15, and 17-18 is proper and respectfully requested.

#### **Response to Claim Rejections Under 35 U.S.C. § 112, Enablement**

Claims 7 and 16 remain rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement based upon the same reasons set forth in the Office Action mailed July 15, 2009.

In addition, the Examiner asserted that the specification is not enabling for any protein from any source, which is 85% identical to the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40 having endoglucanase activity. Applicants' arguments that one skilled in the art would be enabled to make the presently claimed invention based upon the specification and technical knowledge possessed by one skilled in the molecular biology arts, was not found to be persuasive. Specifically, the Examiner asserted that *Ex parte Kubin* (BPAI 2007) does not support Applicants' case because protein of the present application and that of the nucleic acid encoding protein of *Kubin* are different and the fact pattern is not same so that “comparing a decision made by the Board for a particular product cannot be applicable for other product, when the product is completely different.” The Examiner appears to assert that the breadth of the



claimed protein having at least 85% sequence identity to the amino acid sequence of SEQ ID NO: 2, 4, 38, or 40 and having an endoglucanase activity is broad because there would be 15% non-identical proteins of SEQ ID NO: 2, 4, 38, or 40 (i.e., 44 amino acids different out of about 300 amino acids) that “comprise many mutants, variants and recombinants, which may have endoglucanase activity or no activity.” The Examiner states that the present disclosure is limited to the nucleotide and encoded amino acid sequence of only four proteins of SEQ ID NOs: 2, 4, 38 or 40. The Examiner appears to cite to Guo et al. for the proposition that the claimed protein having “at least 85% identity” would result in only 1 active protein from 131 million random mutants.

Initially, Applicants note that the issue and facts of the present case are analogous to that of *Ex parte Kubin*. The Examiner is reminded that application of *Kubin* does not require that the protein of the present invention be identical to the subject protein in the *Kubin* case. In this respect, the present case is similar to the enablement issue and facts presented in *Kubin*. Specifically, the enablement issue in *Kubin* concerned whether undue experimentation would have been required to practice the full scope of the claimed polypeptide having at least 80% identity to amino acids 22-221 of SEQ ID NO:2 and which has the activity to bind CD48. The BPAI noted that the specification in *Kubin* (1) did not disclose any variants in which the amino acids 22-221 of SEQ ID NO:2 was varied, (2) did not disclose which 20% of the amino acid residues should be changed in order to maintain the biological functions for binding CD48, and (3) did not disclose a correlation between the function (binding to CD48) and structure responsible for binding to CD48 (other than the entire extracellular domain) so that a skilled artisan would have known what modifications to could be made of the very large number of modifications potentially encompassed by the claimed protein in *Kubin*. However, the BPAI



noted that specification taught how to make variants of SEQ ID NO:2, calculate the percent identity between SEQ ID NO:2 and the variant sequence, and test the variant sequence to determine if it binds to CD48. The BPAI concluded that based upon the guidance in the specification and the knowledge possessed by one of ordinary skill in the molecular biology art, it would not have required undue experimentation to make the polypeptide having at least 80% identity to amino acids 22-221 of SEQ ID NO:2 and which has the activity to bind CD48. The BPAI noted that although experimentation might have been extensive, it would have routine as the techniques are well known to those skilled in the art.

Nevertheless, and solely to advance prosecution of the present application, the presently claimed isolated protein of (b) is at least 95% identical to the amino acid sequence of SEQ ID NOs: 2, 4, 38, or 40 and has an endoglucanase activity. In this respect, the specification, for example, at page 12-13 and 16-18 teaches the claimed amino acid sequence of SEQ ID NOs: 2, 4, 38, or 40 and production of the same, and how to make the variants of the claimed amino acid sequences as well as calculate the percent identity between the variant sequences and SEQ ID NOs: 2, 4, 38, or 40 at pages 10, 13-15 and pages 18-25. Applicants note that endoglucanase is well-characterized in the art as discussed at pages 6, 8-9, paragraph bridging pages 14-15, paragraph bridging pages 15-16 and shown in Figures 1 and 2 of the specification. As discussed at pages 15-16 of the specification, the catalytic domain and cellulose-binding domain important for endoglucanase activity are well-characterized so that one possessing common technical skill in the molecular biology art may readily make the claimed variant sequences in the catalytic domain, linker region, or cellulose-binding domain and maintain the endoglucanase enzyme activity. Further, page 7 of the specification teaches that endoglucanase activity may be tested by measuring a decrease in the viscosity of a carboxymethylcellulose solution, and that the



endoglucanase activities of wild-type sequences are compared to modified sequences at pages 29-30, 34-35, 37, and 38-40.

Accordingly, the facts and issue of *Ex parte Kubin* are completely applicable to Applicants' claimed invention, and establish that, as recognized by the BPAI, it would not require undue experimentation for one of ordinary skill in the art to make the claimed protein.

With regard to Guo et al. cited by the Examiner, Applicants note that contrary to the Examiner's assertions, "x" is not representative of the number of mutations introduced, and the equation provided by the Examiner at the bottom of page 5 of the present Office Action is not used to determine the percentage of active mutants. Rather, Guo is directed to an "x factor ( $x_{sub}$ )" that represents the probability of protein inactivation with one random amino acid substitution. See page 9205, 1<sup>st</sup> sentence of paragraph bridging 1<sup>st</sup> and 2<sup>nd</sup> column of Guo. Also, this probability factor is calculated from the fractions of mutants (amino acid mutation load frequencies,  $f_n$ ) with (n) number of amino acid changes within a gene-wide randomly mutated library, and from the proportion of mutants that survive functional selection (S). See sentence bridging pages 9205-9206.  $X_{sub}$  is expressed as  $X_{sub} = X_T - i$  in which  $X_T$  is the total protein inactivation probability with random amino acid change and "i" is the indel fraction in the total mutational pool. See page 9206, 1<sup>st</sup> column. Further, Guo examined situations in which amino acid substitutions are tolerated and found that AAG (a 298 amino acid protein; see page 9206, 2<sup>nd</sup> column, 1<sup>st</sup> full paragraph) yielded a total of 920 tolerated amino acid mutations (244 mutant AAG cDNAs) in which the activity of the protein was not inactivated. See page 9207, 2<sup>nd</sup> column 1<sup>st</sup> and 2<sup>nd</sup> paragraph under "Substitutability and Structure" of Guo. Guo found that positions that are evolutionarily conserved are also essential for activity. See page 9207, 2<sup>nd</sup> column, 2<sup>nd</sup> paragraph under "Substitutability and Structure" of Guo.



Thus, for at least the above reasons, one skilled in the art would be enabled to make the presently claimed invention based upon the guidance provided by the disclosure in the specification and the common technical knowledge possessed by one skilled in the molecular biology arts.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, is respectfully requested.

**Response to Claim Rejections Under 35 U.S.C. § 102**

Claims 7 and 16 were rejected under 35 U.S.C. § 102(b) as being anticipated by Rasmussen *et al.* (WO 91/17243 A1).

Rasmussen was asserted to teach a cellulase preparation comprising an endoglucanase enzyme and a gene encoding a cellulase enzyme which is 97.2% identical to the amino acid sequence of SEQ ID NO: 2 of the instant application. Rasmussen is also asserted to teach a vector comprising said nucleic acid encoding cellulase enzyme and a host cell transformed with said nucleic acid and a process for producing said cellulase enzyme in a transformed host cell

Therefore, the Examiner concluded that Rasmussen anticipates claims 7 and 16.

In response, Applicants note that the presently claimed protein wherein the N-terminal amino acid is pyroglutamic acid is not explicitly or inherently disclosed by Rasmussen.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.



## Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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